**REMARKS/ARGUMENTS**

In response to the Office Action of November 28, 2003, Applicant requests re-examination and reconsideration of this application for patent pursuant to 35 U.S.C. 132.

**Support for Amendments/Claim Status**

No new matter has been added by the amendments to the specification.

The Prior Art section has been amended to correct a typographical error found in international application number and to include corresponding international publication number, on page 5, line 1.

No new matter has been added by amendments to claims.

So as to provide Examiner Cheu an opportunity to fully consider all issues, Applicants are filing a Request for Continuing Examination concurrently herewith.

Claims 2-38 were cancelled in a previous reply (September 16, 2003). Claims 1, 39-46 are pending in the instant application. Claims 1, 39 and 44-46 have been amended. Claims 39-46 are withdrawn from consideration. Claim 1 is currently under examination.

Claims 1 and 39 have been amended to clearly indicate the claim does not read on a naturally occurring protein, see page 20, lines 9-16 for support.

Claim 44 has been amended to correspond with the biopolymer

marker of claim 1 (as amended herein). Support for various types of kits can be found in the original disclosure, see, for example, page 36, lines 9-12 and page 47, line 10 to page 48, line 19.

Claims 45 and 46 were amended to provide proper antecedent basis for the term "kit" in claim 44 (as amended herein).

**Restriction**

The Examiner has indicated that newly submitted claims 39-46 (submitted September 16, 2003) are directed to an invention that is independent or distinct from the invention originally claimed for the following reasons: claims 39-43 are directed to methods of diagnosing insulin resistance and claims 44-46 are drawn to kits. The Examiner states that since Applicants have received an action on the merits for the originally presented invention, the invention has been constructively elected by original presentation for prosecution on the merits. Thus, the Examiner has withdrawn claims 39-46 from consideration as being drawn to a non-elected invention.

**Request for Rejoining of Claims**

Considering that claims 39-46 are limited to the use of an isolated biopolymer marker selected from the group consisting of SEQ ID NO: 1, SEQ ID NO: 2, and SEQ ID NO: 3, a search of these claims would encompass this specific biopolymer marker. The instant application is related in claim format to several other applications, both pending and issued, of which serial number 09/846,352 is exemplary. In an effort to maintain equivalent scope

in all of these applications, Applicants respectfully request that the Examiner consider rejoining claims 39-46 in the instant application, which are currently drawn to non-elected inventions, under the decision in *In re Ochiai* (MPEP 2116.01) with claim 1 of the elected invention, upon the Examiner's determination that the claim of the elected invention is allowable and in light of the overlapping search. If the isolated biopolymer marker selected from the group consisting of SEQ ID NO: 1, SEQ ID NO: 2, and SEQ ID NO: 3 is found to be novel, methods and kits limited to its use should also be found novel.

**Rejection under 35 USC 112**

Claim 1, as presented on September 19, 2003, stands rejected under 35 USC 112, first paragraph, as containing subject matter which allegedly was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The Examiner continues to maintain the position that the instant specification, as filed, fails to show that the instantly recited SEQ ID NOS: 1-3 can be unequivocally served as the biomarkers for insulin resistance. The Examiner asserts that the sample size does not appear scientifically reliable to indicate that the claimed biopolymer of are "markers" for insulin resistance and would certainly impose undue burden of experimentation to one

of ordinary skill in the art to use and make the invention.

Applicants respectfully disagree with the Examiner's assertions. Claim 1, as currently amended, specifically recites an isolated biopolymer marker selected from the group consisting of SEQ ID NO:1 (amino acid residues 2-11), SEQ ID NO: 2 (amino acid residues 2-12), SEQ ID NO:3 (amino acid residues 2-13) diagnostic for insulin resistance.

The Examiner appears to believe that since the specification allegedly lacks a certain sample size, it would require undue experimentation for one skilled in the art to make and use the invention. Nevertheless, the Examiner has failed to provide any rationale or evidence showing what sample size one of ordinary skill would consider an adequate sufficient to avoid undue experimentation. The initial burden is upon the Examiner to specifically identify what information is missing and why one skilled in the art could not supply the information without undue experimentation. See MPEP 2164.06(a). References should be supplied if possible to support a *prima facie* case of lack of enablement, see *in re Marzocchi* 439 F.2d 220,224,169 USPQ 367,370 (CCPA 1971); MPEP 2164.04.

Applicants assert that the sample size of a clinical trial does not control the question of enablement. The guidelines for a "test of enablement" indicate that if a statement of utility in the specification contains within it a connotation of how to use, 35

USC 112 is satisfied. The instant application discloses a method for diagnosing insulin resistance through the detection of the claimed biopolymer markers, SEQ ID NOS: 1-3. The data presented in Figures 1, 3 clearly show a positive correlation between the claimed biopolymer markers and insulin resistance. These biopolymer markers have not previously been shown to be associated with insulin resistance. When a marker is discovered to be associated with a disease state, it's potential for diagnostics and/or therapeutics is immediately recognized, even if the involvement of the marker in disease pathology is unknown.

Furthermore, as previously pointed out in the last response by Applicants (page 22, 3rd full paragraph), 8 patient samples were used in the experiment represented by figure 1; 5 diseased samples, and 3 normal samples. Similarly, 8 patient samples were used in the experiment represented by figure 3; 4 diseased samples and 4 normal samples. Thus, the total number of patients being 16 with 5 patients expressing the claimed biopolymers. Sample sizes comprising 5 patients have been deemed adequate for diagnosing insulin resistance. For example, Applicants submit their own patent, US 6,620,786 B1 (Jackowski et al.) which claims a method for diagnosing insulin resistance by detecting the presence of biochemical markers in bodily fluid. Thus, one of skill in the art would conclude the sample size in the present application adequate to avoid undue experimentation.

A declaration by the inventor, George Jackowski, was filed by applicants with the last response (September 16, 2003) to further support the conclusion of enablement. However, it is not clear from the outstanding Office Action (November 28, 2003) whether the Examiner has considered the disclosure therein. A declaration or affidavit is, itself, evidence that must be considered. The Examiner is required to weigh all evidence before him, including the specification and any new evidence supplied by applicant with the evidence and/or sound scientific reasoning previously presented in the rejection and decide whether the claimed invention is enabled. The examiner should **never** make the determination based upon personal opinion. The determination should always be based on the weight of the evidence. See MPEP 2164.05.

As shown by the above arguments, the instant specification, contrary to the Examiner's opinion, does contain proper guidance to enable one of ordinary skill in the art to practice the claimed method for diagnosing insulin resistance without any undue experimentation. Thus, when subjected to the "test for enablement" the Examiner's argument is not sufficient to support the enablement rejection; since the association of the claimed biopolymer marker, SEQ ID NOS: 1-3 with insulin resistance carries with it a connotation of use for diagnostics.

**Rejection under 35 USC 102(b)**

Claims 1, as previously presented, stands rejected under 35 U.S.C. 102(b) as allegedly being anticipated by Borden et al. (WO 96/04790).

The Examiner continues to maintain that Borden et al. teach using mammalian betaine gamma-aminobutyric acid transporter comprising the recited SEQ ID NO: 2 (see SEQ ID NO: 1, residues 583-595). Borden et al. also teach using the markers for screening and diagnosis of GABA associated abnormalities.

Applicants respectfully disagree with the Examiner's assertions. Claim 1, as currently amended, recites specific biopolymer marker peptides, SEQ ID NOS: 1-3, specifically diagnostic for insulin resistance.

SEQ ID NO: 1 as disclosed by Borden et al. contains 2217 residues which encode the entire human betaine/GABA transporter protein while the instant invention is restricted to a fragment comprising 14 residues (SEQ ID NO: 2), of human betaine/GABA transporter protein. Claim 1 recites the phase "consisting of". In contrast to Examiner interpretation of SEQ ID NOS:1-3 as a Markush-type grouping, the phase "consisting of" appears in the a clause of the claim, not the preamble of the claim, it limits the elements set forth in the clause; other elements are not excluded from the claims as a whole (see attached *Mannesmann Demag Corp. v. Engineered Metal Products Co.*, 793 F.2d 1279,230 USPQ 45 (Fed. Cir.

1986 and MPEP 2111.03). Thus, the scope of claim 1 is limited to these specific amino acid residues of SEQ ID NOS: 1-3 diagnostic for insulin resistance.

Accordingly, Applicants respectfully submit that the claim, as instantly presented, now distinguishes over the compositions taught by Borden et al. and respectfully request that this rejection be withdrawn.

Claim 1, as previously presented, stands rejected under 35 U.S.C. 102(b) as allegedly being anticipated by Waterham et al. (Biochemical and Biophysical Research Communications 263:213-218 1999).

The Examiner alleges that Waterham et al. teach cloning human carnitine octanoyl transferase comprising the recited SEQ ID NO:1 (see residues 187-198).

Applicants respectfully disagree with the Examiner's assertions. Claim 1 has been amended to recite specific biopolymer marker peptides (SEQ ID NOS:1-3) specifically diagnostic for insulin resistance. Thus, claim 1 recites these specific peptides with a specific function or use.

Waterham et al. teach a 613 residue sequence in Figure 1 which encodes the entire human carnitine octanoyl transferase while the instant invention disclose a 12 residue fragment of human carnitine octanoyl transferase. Claim 1 has been amended to recite the phrase "consisting of". Since "consisting of" is closed

language and excludes any element, step or ingredient not specified in the claim (see MPEP 2111.03), the scope of the instant claim now encompasses only these specific peptides(SEQ ID NO:1, SEQ ID NO:2 and SEQ ID NO:3)having this specific function (diagnostic for insulin resistance), thus excluding the sequences as described by Waterham et al.

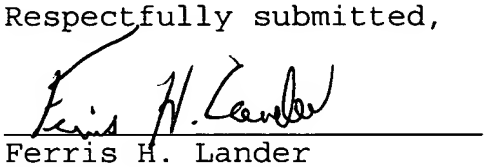
Furthermore, no where does Waterham et al. teach the claimed fragment of SEQ ID NO:1. Nor does Waterham et al. teach that their sequence or any fragment thereof is diagnostic for insulin resistance.

Accordingly, Applicants respectfully submit that claim 1, as instantly presented, now distinguishes over the compositions taught by Waterham et al. and respectfully request that this rejection now be withdrawn.

SUMMARY

In light of the foregoing remarks and amendment to the claims, it is respectfully submitted that the Examiner will now find the claims of the application allowable. Favorable reconsideration of the application is courteously requested.

Respectfully submitted,



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